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(71) Applicant *(for all designated States except US)*: CANCER RESEARCH VENTURES LIMITED [GB/GB]; Cambridge House, 6–10 Cambridge Terrace, Regent's Park, London NW1 4JL (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: PELICCI, Pier, Giuseppe [IT/IT]; Istituto Europeo di Oncologia, Dipartimento di Oncologia Sperimentale, Via Ripamonti, 435, I–20141 Milan (IT). GIORGIO, Marco [IT/IT]; Istituto Europeo di Oncologia, Dipartimento di Oncologia Sperimentale, Via Ripamonti, 435, I–20141 Milan (IT). MIGLIACCIO, Enrica [IT/IT]; Istituto Europeo di Oncologia, Dipartimento di Oncologia Sperimentale, Via Ripamonti, 435, I–20141 Milan (IT). LANFRANCONE, Luisa [IT/IT]; Istituto Europeo di Oncologia, Dipartimento di Oncologia Sperimentale, Via Ripamonti, 435, I–20141 Milan (IT).

(74) Agents: CRIPPS, Joanna, E. et al.; Mewburn Ellis, York House, 23 Kingsway, London WC2B 6HP (GB).

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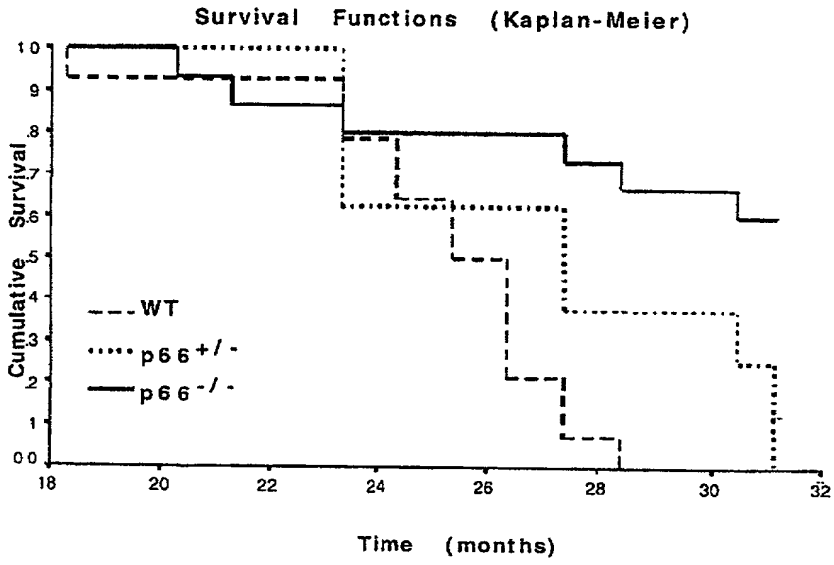

(57) Abstract

It has been determined that i) $p66^{shc}$ is serine phosphorylated upon UV treatment or oxidative damage; ii) the serine–phosphorylation of p66 by oxidative signals is mediated by Erk1 and p38, as shown both in vivo and in vitro; iii) ablation of $p66^{shc}$ expression by homologous recombination enhances resistance to oxidative damage both *in vitro* and *in vivo*; iv) a serine–phosphorylation defective mutant of $p66^{shc}$ is unable to restore a normal stress response in $p66^{shc}$ targeted cells; v) mice carrying the $p66^{shc}$ targeted mutation have prolonged lifespan.